Continental J. Medical Research 5 (1): 19 - 21, 2011 ISSN: 2141 – 4211
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` Printed in Nigeria

MANAGEMENT OF PREGNANCY ASSOCIATED BREAST CANCER WITH CHEMOTHERAPY ADJUVANT

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ABSTRACT
Pregnancy associated breast cancer is cancer occurring during pregnancy and up to one year post delivery. Local oncologists have strong reservations about administering adjuvant chemotherapy for gestational breast cancer. We present a 31 year old University graduate with early left breast cancer in first trimester that had adjuvant chemotherapy administered from the second trimester. She had a normal vaginal delivery at 37 weeks with good apgar scores of baby. Birth defects or discernible malformations were not noted. The safety of adjuvant chemotherapy from second trimester is documented in the literature.

KEYWORDS: Breast cancer, Pregnancy, Birth defects, chemotherapy

INTRODUCTION: Breast cancer is the unenviable captain of cancers in Nigerian women. Mortality rates are high consequent on a high rate of advanced tumours. While the reasons for this trend are numerous, oncologist still need to fashion out ways of dealing with this ravaging scourge of Nigerian women. With a high rate of premenopausal cancer, a minority of women in this fertile group, are diagnosed with the disease. Pregnancy associated breast cancer or gestational breast cancer is cancer occurring during pregnancy and up to one year post delivery (Loibl *et al*., 2006). It is a rare occurrence, crude incidence rates of 1 in 3000 pregnancies haven been described from Western studies (Loibl *et al*., 2006). Despite a low incidence, it has the reputation of being the most common gestational cancer, second only to cervical cancer (Loibl *et al*., 2006). Due to its obstetric association, oncologists have to balance the issues of health of the fetus competing against optimal cancer treatment. Anecdotal observations suggest that local oncologists have strong reservations about administering chemotherapy in pregnancy associated breast cancer. We are not aware of any reported case in the local literature, of chemotherapy administration for gestational breast cancer.
This has prognostic implications for the disease.

We present a 31 year old University graduate, that presented with a two month history of a right breast lump, diagnosed as early breast cancer at 13 weeks gestation, managed yet with conserving breast surgery and chemotherapy adjuvant. Pregnancy and delivery were uneventful with no discernible defects of the baby.

JI, presented with a two months history of a painless right breast lump. Menarche was at 13 years. She had a yet only confinement at 29 years. Breastfeeding history was for eight months. There was no family history of breast cancer. She had three months secondary amenorrhoea. Examination showed a young lady that was not pale and anicteric. Breast exam showed a circumareolar scar in the right breast with an associated lump, two centimeters in largest diameter. The right axilla had no palpable lymph node. The left breast and axilla were unremarkable. Abdominal ultrasound showed a viable fetus at 14 weeks gestation. Histopathology had revealed an invasive lobular carcinoma. An assessment of early breast carcinoma was made. After treatment options were explained, She had a wide local excision of the surgical bed and chemotherapy was commenced with Adriamycin 50mg/m2, cyclophosphamide 500mg/m2 and 5-fluorouracil regimen 500mg/m2. A 72 hour continous infusion protocol was used for adriamycin following the third up to the fifth cycle. This regimen was repeated at three weekly intervals. Serial obstetric ultrasound monitoring following chemotherapy sessions, showed a well developing fetus with no evidence of growth retardation. A fifth cycle was administered at 32 weeks gestation and a break observed before delivery. She was delivered of a male baby at 37 weeks gestation after she fell into spontaneous labour. Apgar score was 8/1 and 10/5 minutes. Birth weight was 3.5kg. No birth defects or discernible malformations have been noted. Patient has shown good response to treatment so far.

DISCUSSION

EARLY versus LATE PRESENTATION

Our case presented with gestational breast cancer at age 31 years. The mean age at presentation has been described at 32-34 years (Middleton *et al*., 2003). The cancer was considered early at presentation even though radiological screening tests could not be done. This contrasts against the report of other researchers, pregnancy associated breast cancer patients being diagnosed with larger tumours and lymph node metastases (Woo *et al.,* 2003*).* Our case was a tertiary education recipient, which must have been a factor in her earlier presentation; not very usual in breast cancer patients seen locally. The enlargement and engorgement of the breast associated with pregnancy, has been linked with delayed diagnosis for patient and Physician alike. We think that regular breast exam practitioners may be spared this unfortunate oversight, being more accustomed with their breasts regardless of physiological changes.

TREATMENT

Our case had successful breast cancer treatment without terminating pregnancy. Contrary to previous ideas, therapeutic abortion is no longer considered an option (Barnes and Newman, 2007). The ideas had been borne following a fatalistic approach which attended the management of this condition. This was thought to be due to rapid growth of the tumour from the influence of an increased hormonal milieu. Contrary to earlier perceptions of pregnancy being a poor prognostic factor, results have shown similar outcomes when pregnant patients with early breast cancer were matched for age and stage with non-pregnant ones (Anderson *et al.,* 1996) Earlier arguments of the hormonal milieu affecting outcome has not been proven (Melnick, 2004).

Our case had breast conserving surgery as against mastectomy which has been largely favoured classically. Although this has the advantage of making radiotherapy unnecessary considering the fetus, it is unattractive to young women as our case. In line with the current trend towards less ablative surgeries, breast conserving surgeries has been increasingly offered for early cancer to these young women (Barnes and Newman, 2007). This is less mutilating and can be done with local anaesthesia and sedation as in our case. The same cannot be said of mastectomy with a risk of abortion, highest during the first trimester (Woo *et al.,* 2003*).*

CHEMOTHERAPY

Chemotherapy being an important adjuvant in breast cancer treatment was utilized from the 14 weeks gestation. This is in keeping with evidence that documents a good safety profile with chemotherapy administered after the first trimester inspite of the teratogenic potential of cytotoxics (Woo *et al., (*2003*); (*Hahn *et al.,* 2007) Documented incidences of fetal malformations following chemotherapy outside first trimester is low at 1.3% compared with 14-19% for chemotherapy administered during the first trimester (Doll *et al.,* 1989). Hahn *et al* have reported the largest series involving 57 pregnancy associated breast cancer patients that had chemotherapy in second and third trimester. They reported no attendant miscarriages, stillbirths or perinatal deaths related to therapy (Woo *et al., (*2003*).* However unlike our case that had a normal birth weight at 3.5 kg and no perinatal complications so far, this large series recorded six cases of low birth weight. Difficulty in breathing was the most common complication. However, no perinatal deaths were recorded and developmental milestones appeared uneventful. We suggest that management of gestational breast cancer should be in a good quality centre with appropriate interspecialty collaboration.

Anthracycline based chemotherapy was employed in our case. Doxorubicin has shown a better safety in pregnancy than epirubicin; epirubicin has been associated with intrauterine fetal deaths and neonatal cardiac effects (Giacalone *et al,* 1999). Continous infusion protocol over 72 hours as in the series by Hahn *et al,* was employed from the third course. Our case had much less chemotherapy side effects of vomiting and weakness compared to previous cycles with a bolus administration over one hour. This is a useful finding in an environment where patients ignore the benefits and default or even abandon chemotherapy over these discomforting side effects. Additionally, researchers have demonstrated no differences in systolic function in adriamycin exposed fetuses and unexposed both inutero and up to two years postnatal (Meyer-Wittkopf *et al,* 2001).

Tamoxifen is not recommended due to its teratogenic properties of ambiguous genitalia (Barthelmes and , Gateley, (2004), (Loibl *et al*., 2006). However there are opposing case reports suggesting safe outcome following its use (Barthelmes and Gateley, (2004). We observed good oncologic response following chemotherapy and surgery alone and opine that in view of teratogenicity documentations but good results with

surgery and chemotherapy, it should be deferred till delivery. Our patient had a four week chemotherapy break before expected date of delivery. This is following the recommendations of avoiding chemotherapy at this time in order to reduce incidences of pancytopaenia and infections in the neonate (Woo *et al.*, 2003*).*

RADIOTHERAPY

Our case is being scheduled for radiotherapy having successful delivery. Radiotherapy is considered contraindicated in all three trimesters. We opine that surgery and cyclical chemotherapy at three to four weekly intervals, spans the entire pregnancy and should provide local control of the disease pending postnatal radiotherapy, as in our case. However a minority report from workers, have reported successful cases of pregnant patients being irradiated for Hodgkins lymphoma. They assert that the risks of radiotherapy were exaggerated as they are significant during the first trimester. They maintain that with appropriate abdominal shielding of the fetus, the fetal radiation exposure was too minimal to cause damage (Kal and Struikmans, 2006).

RECOMMENDATION

We recommend adjuvant chemotherapy in the management of pregnancy associated breast cancer from the second trimester.

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Received for Publication: 26/04/11, Accepted for Publication: 10/05/11